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EXAMINER

BAUM, STUART F

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1638 | |

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/019,931

Applicant(s)

VARIN ET AL.

Examiner

Stuart F. Baum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/29/2006, 5/1/2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 59-73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 59-73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/29/2006.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

RCE Acknowledgment

1. The request filed on 3/29/2006 for a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114, based on parent Application No. 10/019,931 is acceptable and a RCE has been established. An action on the RCE follows.
2. The amendments filed 3/29/2006 and 5/1/2006 have been entered.
3. Claims 59-73 are pending.

Claims 59-73 have been newly added.

Claims 1-2, 6-9, 43, 47, and 52-58 have been canceled.
4. Claims 59-73, including SEQ ID NO:1 encoding SEQ ID NO:3, are examined in the present office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 59-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

Claims 59, 60, 63, 65, and 67 are indefinite for reciting "similarity". Applicants use this term to describe both nucleic acid sequences and amino acid sequences. The specification defines "similarity" in the context of nucleic acid sequences that are hybridizable under low or high stringency (page 11, lines 8-17). The definition does not clarify the meaning because

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Applicants do not recite any hybridizing conditions that exemplify low or high stringency. In addition, Applicants do not define “similarity” in regards to amino acid sequences. Therefore, the Office contends that the term “similarity” carries no weight.

Claims 59 and 62 are indefinite for reciting “functional homologue”. Applicants define “functional homologue” as a protein or nucleic acid sequence encoding an enzyme having a substantially similar biological activity as 11- or 12-hydroxyjasmonate sulfotransferase and isoenzymes thereof (sentence bridging pages 8 and 9). Applicants have not defined the metes and bounds of substantially similar and therefore one skilled in the art would not be appraised of the upper and lower limits of activities that are encompassed by substantially similar biological activities.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 70-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite “which is cauliflower”, “which is broccoli”, and “which is a horticultural plant”. Applicants fail to point to support for the phrase in the instant

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specification. Upon a cursory search of the specification, support could not be found.

Applicants are required to point to support for “which is cauliflower”, “which is broccoli”, and “which is a horticultural plant” or to amend the claims to delete the NEW MATTER.

Written Description

7. Claims 59-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for accelerating flowering in a plant comprising altering the level of at least one compound listed in claims 59 by expression of a functional homologue of sulfotransferase encoded by SEQ ID NO:1 having at least 80% similarity to SEQ ID NO:1, or wherein the sulfotransferase has an amino acid sequence having at least 80% similarity to SEQ ID NO:3, or a method for producing a transgenic plant which flowers early comprising introducing into a cell an exogenous nucleic acid molecule comprising a nucleotide sequence antisense to a nucleic acid sequence coding for an amino acid sequence having at least 80% similarity to SEQ ID NO:3, encoding a plant hydroxyjasmonic acid sulfotransferase, or wherein the method further comprises the step of inhibiting in said plant the expression of a functional homologue having at least 80% similarity to SEQ ID NO:1.

Because of the 112 second indefiniteness of “similarity” as discussed above, the Office contends the recitation “similarity” carries no weight and broadly interprets the claims to read on

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any nucleic acid sequence encoding any protein having biological activity or any amino acid sequence having biological activity.

Applicants define “functional homologue” as a protein or nucleic acid sequence encoding an enzyme having a substantially similar biological activity as 11- or 12-hydroxyjasmonate sulfotransferase and isoenzymes thereof (sentence bridging pages 8 and 9). Applicants have not explicitly defined a substantially similar biological activity of said enzymes and therefore, the Office contends the recitation “functional homologue” carries no weight.

Applicants disclose a nucleic acid sequence encoding an Arabidopsis 12-hydroxyjasmonic acid sulfotransferase (AtST2a) of SEQ ID NO:1 (page 5, line 13-17 and page 6, lines 29-32).

Applicants do not identify essential regions of the protein encoded by SEQ ID NO:1, nor do Applicants disclose any polynucleotides encoding any polypeptides that are functional homologues of any sulfotransferase that can be used to alter the level of any compound listed in claim 59.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, “A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined

by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.” *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences from a representative number of plant species encoding a sulfotransferase capable of altering the level of any compound listed in claim 59. Applicants only describe a single cDNA sequence of SEQ ID NO:1. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the protein encoded by SEQ ID NO:1, it remains unclear what features identify an *Arabidopsis* hydroxyjasmonic acid sulfotransferase protein. Since the genus of hydroxyjasmonic acid sulfotransferase proteins has not been described by specific structural features the specification fails to provide an adequate written description to support the breadth of the claims.

Scope of Enablement

8. Claims 59-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the time to flowering in *Arabidopsis* plants comprising transforming said plants with the *Arabidopsis* AtST2a genomic sequence of SEQ ID NO:1, operably linked to a promoter in antisense orientation, wherein the levels of 12- or 11-hydroxyjasmonic acid are increased relative to non-transgenic plants, does not reasonably provide enablement for any method that accelerates flowering in a plant comprising modifying

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the endogenous level of at least one of any of the compounds listed in claim 59, or a method for producing a transgenic plant which flowers early comprising expressing a sulfotransferase encoded by SEQ ID NO:1 or a functional homologue having at least 80% similarity to SEQ ID NO:1, or comprising a sequence that is antisense to a nucleic acid of SEQ ID NO:1 or antisense to a nucleic acid sequence which is a functional homologue having at least 80% similarity to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to a method for accelerating flowering in a plant comprising altering the level of at least one compound listed in claims 59 by expression of a functional homologue of sulfotransferase encoded by SEQ ID NO:1 having at least 80% similarity to SEQ ID NO:1, or wherein the sulfotransferase has an amino acid sequence having at least 80% similarity to SEQ ID NO:3, or a method for producing a transgenic plant which flowers early comprising introducing into a cell an exogenous nucleic acid molecule comprising a nucleotide

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sequence antisense to a nucleic acid sequence coding for an amino acid sequence having at least 80% similarity to SEQ ID NO:3, encoding a plant hydroxyjasmonic acid sulfotransferase, or wherein the method further comprises the step of inhibiting in said plant the expression of a functional homologue having at least 80% similarity to SEQ ID NO:1.

Because of the 112 second indefiniteness of “similarity” as discussed above, the Office contends the recitation “similarity” carries no weight and broadly interprets the claims to read on any nucleic acid sequence encoding any protein having biological activity or any amino acid sequence having biological activity.

Applicants define “functional homologue” as a protein or nucleic acid sequence encoding an enzyme having a substantially similar biological activity as 11- or 12-hydroxyjasmonate sulfotransferase and isoenzymes thereof (sentence bridging pages 8 and 9). Applicants have not explicitly defined a substantially similar biological activity of said enzymes and therefore, the Office contends the recitation “functional homologue” carries no weight.

Applicants disclose a nucleic acid sequence encoding an Arabidopsis 12-hydroxyjasmonic acid sulfotransferase (AtST2a) of SEQ ID NO:1 (page 5, line 13-17 and page 6, lines 29-32). Applicants subcloned SEQ ID NO:1 into a vector comprising two CaMV 35S minimal promoters operably linked in antisense orientation (page 25, lines 13-14). The resulting construct was transformed into Arabidopsis which produced plants that had a lower level of endogenous hydroxyjasmonic acid sulfotransferase and 12-hydroxyjasmonate sulfate and flowered earlier compared to plant not transformed with said construct. Said plants also had a higher level of 12-hydroxyjasmonate compared to non-transgenic plants (page 29, lines 10-29).

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The state-of-the-art teach transforming a plant with a nucleic acid molecule encoding a protein involved in jasmonic acid biochemistry does not lead to predictable results. Harms et al (1995, *The Plant Cell* 7:1645-1654) teach potato plants transformed with a nucleic acid sequence encoding an allene oxide synthase (AOS) which converts lipoxygenase-derived fatty acid hydroperoxide into the precursor for jasmonic acid formation. Harms et al disclose that overexpression of the AOS cDNA produced plants that had six to twelve fold higher levels of jasmonic acid compared to non-transformed plants but the transgenic plants did not exhibit increased levels of other genes which are normally induced during increased levels of jasmonic acid caused by wounding (abstract). In short, jasmonic acid-responding genes were not induced when jasmonic acid levels were increased.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that are 80% similar to SEQ ID NO:1 will encode a protein with the same activity as a protein encoded by SEQ ID NO:1. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, *Science* 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, *Nature* 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

The state-of-the-art teach that antisense technology produces unpredictable results. Bryant (1989, Trends in Biotechnology 7(2):20-21) teaches using antisense to downregulate chalcone synthase did not always produce plants with the desired result. It was not clear why plants were produced with all levels of regulated chalcone synthase, from plants exhibiting suppression to plants exhibiting a wild-type phenotype (page 20, right column, 1st paragraph). Bryant suggests that “position effect” influences transgene expression (page 20, right column, 2nd paragraph). In addition, using sequences that are not 100% identical to the target sequence will not produce expected results. Emery et al (2003, Current Biology 13:1768-1774) disclose experiments in which a target sequence of a micro-RNA was changed by two base-pairs. The altered base-pairs caused the complementary micro-RNA not to bind to the target sequence, which subsequently led to an increased expression of the target sequence’s encoded protein (page 1769, right column, 2nd full paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants’ broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

Re: claim 59 recites “modifying” and “altered” in regards to a level of an endogenous compound listed in claim 59. “Modifying” and “alter” encompass both increases and decreases in levels and Applicants have only produced plants that had a lower level of endogenous hydroxyjasmonic acid sulfotransferase and 12-hydroxyjasmonate sulfate. Applicants are not enabled for “modifying” or “alter”.

Re: claim 64 recites “applying to a plant” one of the compounds listed in claim 64. Applicants have not applied any of the compounds to a plant to produce a plant that flowers early, especially in light of the method of claim 59 in which the levels of said compounds is reduced in order to produce a plant that flowers early.

Re: claim 66 recites increasing the endogenous levels of a hydroxylase which hydroxylates jasmonic acid or methyljasmonic acid. Applicants have not disclosed by way of guidance or examples any methods for increasing the levels of said hydroxylase in a plant. Applicants have not disclosed how the methods of claims 59 or 62 affect hydroxylase activity and in turn affect jasmonic acid or methyljasmonic acid. Therefore, claim 66 is not enabled.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:1 as probes or by designing primers to undisclosed regions of SEQ ID NO:1 and isolating or amplifying fragments, subcloning the fragments in antisense orientation, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when transcribed in the plant, reduce the endogenous levels of any of the compounds listed in claim 59 and cause the plant to flower early when compared to a non-transgenic plant.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 59-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Weigel (December, 1998, U.S. Patent Number 5,844,119).

The claims are drawn to a method for accelerating flowering in a plant, comprising modifying in said plant an endogenous level of 12-hydroxyjasmonic acid, sulfate ester of 12-hydroxyjasmonic acid, 11-hydroxyjasmonic acid, sulfate ester of 11-hydroxyjasmonic acid, and mixtures thereof, wherein the endogenous level of at least one of the before mentioned compounds is altered by expression of a sulfotransferase functional homologue having at least 80% similarity to SEQ ID NO:1, or wherein the sulfotransferase functional homologue has at least 80% similarity to SEQ ID NO:3, or wherein the plant is transgenic.

Because of the 112 second indefiniteness of “similarity” as discussed above, the Office contends the recitation “similarity” carries no weight and broadly interprets the claims to read on any nucleic acid sequence encoding any protein having biological activity or any amino acid sequence having biological activity.

Applicants define “functional homologue” as a protein or nucleic acid sequence encoding an enzyme having a substantially similar biological activity as 11- or 12-hydroxyjasmonate sulfotransferase and isoenzymes thereof (sentence bridging pages 8 and 9). Applicants have not explicitly defined a substantially similar biological activity of said enzymes and therefore, the Office contends the recitation “functional homologue” carries no weight.

Weigel discloses a transgenic plant that has accelerated flower meristem development and methods to produce said plant (columns 21-24, claims 1-28). The Office interprets

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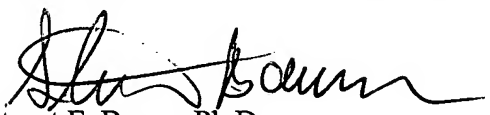
“accelerated flower meristem development” to mean a plant that flowers early or has accelerated flowering. Because of the indefiniteness of “functional homologue” and “similarity” as discussed above, Applicants’ claims read on any transgenic plant that flowers early, because it would be inherent that said early flowering plant would have an altered expression of a gene that is in any way similar to SEQ ID NO:1, and if the plant is flowering early, then any of the compounds listed in claim 1 would also be modified, and as such, Weigel anticipates the claimed invention.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Anne Marie Grunberg can be reached at 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.


Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
May 12, 2006

STUART F. BAUM, PH.D.
PATENT EXAMINER